CLAIMS

What is claimed is:

1. An isolated DNA encoding a 4-1BB-L polypeptide, wherein said DNA comprises a nucleotide sequence selected from the group consisting of nucleotides 53-979 of the murine 4-1BB-L sequence of SEQ ID NO:1 and nucleotides 4-765 of the human 4-1BB-L sequence of SEQ ID NO:3.

2. An isolated DNA encoding a 4-1BB-L polypeptide, wherein said DNA is degenerate as a result of the genetic code to a nucleotide sequence of claim 1.

3. An isolated DNA capable of hybridizing to a nucleotide sequence of claim 1 under moderately stringent conditions, wherein said DNA encodes a 4-1BB-L polypeptide capable of binding to 4-1BB.

4. An isolated DNA of claim 3, wherein said DNA encodes a soluble 4-1BB-L polypeptide.

5. An isolated DNA of claim 4, wherein said DNA additionally encodes an antibody Fc polypeptide fused to the C-terminus of said soluble 4-1BB-L polypeptide.

6. An isolated DNA of claim 4 wherein the soluble 4-1BB-L polypeptide is a soluble human 4-1BB-L polypeptide comprising amino acids 49-254 of SEQ ID NO:3.

7. A recombinant expression vector comprising a DNA according to claim 1 operably linked to regulatory sequences suitable for expression of said DNA in a host cell.

8. A recombinant expression vector comprising a DNA according to claim 2 operably linked to regulatory sequences suitable for expression of said DNA in a host cell.

9. A recombinant expression vector comprising a DNA according to claim 3 operably linked to regulatory sequences suitable for expression of said DNA in a host cell.

10. A recombinant expression vector comprising a DNA according to claim 4 operably linked to regulatory sequences suitable for expression of said DNA in a host cell.

11. A recombinant expression vector comprising a DNA according to claim 5 operably linked to regulatory sequences suitable for expression of said DNA in a host cell.

12. A process for preparing a 4-1BB-L polypeptide, comprising culturing a host cell comprising a vector according to claim 7 under conditions that promote expression of the 4-1BB-L polypeptide, and purifying the 4-1BB-L polypeptide.

13. A process for preparing a 4-1BB-L polypeptide, comprising culturing a host cell comprising a vector according to claim 8 under conditions that promote expression of the 4-1BB-L polypeptide, and purifying the 4-1BB-L polypeptide.

14. A process for preparing a 4-1BB-L polypeptide, comprising culturing a host cell comprising a vector according to claim 9 under conditions that promote expression of the 4-1BB-L polypeptide, and purifying the 4-1BB-L polypeptide.

15. A process for preparing a soluble 4-1BB-L polypeptide, comprising culturing a host cell comprising a vector according to claim 10 under conditions that promote expression of the 4-1BB-L polypeptide, and purifying the 4-1BB-L polypeptide.

16. A process for preparing a soluble 4-1BB-L/Fc fusion protein, comprising culturing a host cell comprising a vector according to claim 11 under conditions that promote expression of the 4-1BB-L/Fc fusion protein, and purifying said fusion protein.

17. A purified 4-1BB ligand polypeptide (4-1BB-L) comprising an N-terminal amino acid sequence selected from the group consisting of Met-Glu-Tyr-Ala-Ser-Asp-Ala-Ser-Leu-Asp-Pro-Glu-, Leu-Ala-Cys-Pro-Trp-Ala-Val-Ser-Gly-Ala-Arg-Ala-Ser-, Met-Asp-Gln-His-Thr-Leu-Asp-Val-Glu-Asp-Thr-Ala-, Arg-Thr-Glu-Pro-Arg-Pro-Ala-Leu-Thr-Ile-Thr-Thr-, Thr-Glu-Pro-Arg-Pro-Ala-Leu-Thr-Ile-Thr-Thr-, and Glu-Pro-Arg-Pro-Ala-Leu-Thr-Ile-Thr-Thr-.

18. A purified 4-1BB-L according to claim 17, comprising an amino acid sequence selected from the group consisting of amino acids amino acids 1-254 of SEQ ID NO:3, amino acids 49-254 of SEQ ID NO:3, amino acids 1-309 of SEQ ID NO:1, and amino acids x-309 of SEQ ID NO:1, wherein x is selected from the group consisting of 104, 105, and 106.

19. A purified 4-1BB-L according to claim 17, comprising an amino acid sequence that is identical to a sequence selected from the group consisting of amino acids amino acids 1-254 of SEQ ID NO:3, amino acids 49-254 of SEQ ID NO:3, amino acids 1-309 of SEQ ID NO:1, and amino acids x-309 of SEQ ID NO:1, wherein x is selected from the group consisting of 104, 105, and 106, except for conservative amino acid substitution(s).

20. A purified 4-1BB-L polypeptide wherein said polypeptide is encoded by a DNA selected from the group consisting of:

(a) DNA comprising a nucleotide sequence selected from the group consisting of nucleotides 53-979 of the murine 4-1BB-L sequence of SEQ ID NO:1 and nucleotides 4-765 of the human 4-1BB-L sequence of SEQ ID NO:3;

(b) DNA capable of hybridizing to a DNA of (a) under moderately stringent conditions and which encodes a 4-1BB-L capable of binding to a 4-1BB; and

(c) DNA which, due to the degeneracy of the genetic code, encodes a 4-1BB-L polypeptide encoded by a DNA of (a).

21. A purified 4-1BB-L of claim 20 wherein said 4-1BB-L is a soluble 4-1BB-L polypeptide.

22. A purified soluble 4-1BB-L of claim 21 which additionally comprises an antibody Fc polypeptide fused to the C-terminus of said soluble 4-1BB-L polypeptide.

23. A purified soluble human 4-1BB-L comprising the amino acid sequence of amino acids 49-254 of SEQ ID NO:4.

24. A pharmaceutical composition comprising an effective amount of a soluble human 4-1BB-L of claim 21 in admixture with a suitable diluent, carrier, or excipient.

25. A dimer comprising two soluble 4-1BB-L polypeptides of claim 22, joined *via* disulfide bonds between the Fc polypeptides fused to said soluble 4-1BB-L polypeptides.

Sub B2 26. An antibody that is immunoreactive with a 4-1BB-L polypeptide of claim 20.

27. An antibody of claim 26, wherein said antibody is a monoclonal antibody.

28. An isolated nucleic acid molecule comprising a sequence of at least about 17 nucleotides of a DNA sequence according to claim 1 or its DNA or RNA complement.

29. An isolated DNA encoding a human 4-1BB polypeptide, wherein said DNA comprises a nucleotide sequence selected from the group consisting of:

a) nucleotides 120-884 of SEQ ID NO:7;

b) nucleotides 189-884 of SEQ ID NO:7; and

c) a nucleotide sequence that is degenerate as a result of the genetic code to a nucleotide sequence of (a) or (b).

30. An isolated DNA encoding a soluble human 4-1BB polypeptide, wherein said polypeptide comprises the extracellular domain of human 4-1BB (amino acids 1-163 of SEQ ID NO:7) or a fragment thereof capable of binding a 4-1BB-L.

31. An isolated DNA of claim 30, wherein said DNA additionally encodes an antibody Fc polypeptide fused to the C-terminus of said soluble human 4-1BB polypeptide.

32. A recombinant expression vector comprising a DNA ~~sequence~~ according to claim 29 operably linked to regulatory sequences suitable for expression of said DNA sequence in a host cell.

33. A recombinant expression vector comprising a DNA ~~sequence~~ according to claim 30 operably linked to regulatory sequences suitable for expression of said DNA sequence in a host cell.

34. A recombinant expression vector comprising a DNA ~~sequence~~ according to claim 31 operably linked to regulatory sequences suitable for expression of said DNA sequence in a host cell.

35. A process for preparing a human 4-1BB polypeptide, comprising culturing a host cell comprising a vector according to claim 32 under conditions that promote expression of the human 4-1BB polypeptide, and purifying said polypeptide.

36. A process for preparing a soluble human 4-1BB polypeptide, comprising culturing a host cell comprising a vector according to claim 33 under conditions that promote expression of the human 4-1BB polypeptide, and purifying said polypeptide.

37. A process for preparing a fusion protein comprising an antibody Fc polypeptide fused to the C-terminus of a soluble human 4-1BB polypeptide, comprising

culturing a host cell comprising a vector according to claim 34 under conditions that promote expression of the human fusion protein, and purifying said fusion protein.

38. A purified human 4-1BB polypeptide comprising the N-terminal amino acid sequence Leu-Gln-Asp-Pro-Cys-Ser-Asn-Cys-Pro-Ala-Gly-Thr-.

39. A purified 4-1BB according to claim 38, comprising an amino acid sequence selected from the group consisting of amino acids 1-232 of SEQ ID NO:7 and amino acids 1-163 of SEQ ID NO:7.

40. A purified 4-1BB according to claim 38, comprising an amino acid sequence that is identical to a sequence selected from the group consisting of amino acids 1-232 of SEQ ID NO:7 and amino acids 1-163 of SEQ ID NO:7, except for conservative amino acid substitution(s).

41. A purified soluble human 4-1BB polypeptide, wherein said polypeptide comprises the extracellular domain of human 4-1BB (amino acids 1-163 of SEQ ID NO:7) or a fragment thereof capable of binding a 4-1BB-L.

42. A purified soluble human 4-1BB polypeptide of claim 41, additionally comprising an antibody Fc polypeptide fused to the C-terminus of said human 4-1BB polypeptide.

43. A dimer comprising two soluble human 4-1BB polypeptides of claim 42, joined *via* disulfide bonds between the Fc polypeptides fused to said soluble 4-1BB polypeptides.

44. A pharmaceutical composition comprising an effective amount of a soluble human 4-1BB of claim 41 in admixture with a suitable diluent, carrier, or excipient.

45. An antibody that is immunoreactive with a human 4-1BB polypeptide of claim 38.

46. An antibody of claim 45, wherein said antibody is a monoclonal antibody.

47. An isolated nucleic acid molecule comprising a sequence of at least about 30 nucleotides of a DNA sequence according to claim 29 or its DNA or RNA complement.